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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,050	10/12/2004	Masami Kusaka	Q101060	6207

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EXAMINER	
HUYNH, CARLIC K	
ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
09/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/511,050	KUSAKA ET AL.	
	Examiner	Art Unit	
	Carlic K. Huynh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *1 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *21 July 2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-8 are pending in the application, with claims 1 and 8 having been withdrawn, in response to the restriction requirement made by telephone on August 1, 2007. It is noted claims 2-6 have been amended for inclusion into Group II, in the Response to Election/Restriction filed on August 17, 2007. Accordingly, claims 2-7 are being examined on the merits herein.

Election/Restrictions

2. Applicant's election without traverse of the claims of Group II, claim 7 was made by telephone to the Applicants' Representative, Mike Dzwonczyk, on August 1, 2007.

Claims 2-6 have been amended for inclusion into Group II, in the reply filed on August 17, 2007.

Claims 1 and 8 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse by telephone call on August 1, 2007 and in the reply filed on August 17, 2007.

Accordingly, Group II, now claims 2-7, are being examined on the merits herein.

The election/restriction requirement is deemed proper and is made FINAL.

Information Disclosure Statement

The Information Disclosure Statement submitted on July 21, 2005 is acknowledged.

Specification

3. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

The abstract contains legal phraseology, namely "said". Appropriate correction is required. See MPEP 37 CFR § 1.72 (b).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating hot flash, does not reasonably provide enablement preventing hot flash. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan

to fully practice the instant invention without ***undue experimentation***. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors:
(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1). ***Nature of the Invention***:

The rejected claim(s) is/are drawn to an invention which pertains to a method for preventing or treating hot flash comprising administering a non-peptidic compound having gonadotropin releasing hormone antagonistic activity.

(2). ***State of the Prior Art***:

The skilled artisan would view that the prevention of hot flash is highly unlikely. If fact the prior art acknowledges that the cause of hot flashes is not clear although a decrease in sex hormone levels trigger it (page 2, lines 5-7 of the specification).

(3). ***Relative Skill of Those in the Art***:

The relative skill of those in the art of hot flash is extremely high.

(4). ***Predictability of the Art***:

The prevention of hot flash is highly unpredictable. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and that physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Thus, the state of the art is highly unpredictable.

(5). ***Breadth of the Claims***:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass a method for preventing or treating hot flash comprising administering a non-peptidic compound having gonadotropin releasing hormone antagonistic activity.

(6). ***Direction or Guidance Presented***:

The guidance given by the specification as to a method of preventing hot flash comprising administering a gonadotropin releasing hormone antagonist is limited.

The disclosure of a method of treating hot flash comprising administering a gonadotropin releasing hormone antagonist is adequate (page 97, Experimental Example 2).

(7). ***Working Examples***:

The working examples in the specification show treatment with Reference Example 7, a gonadotropin-releasing hormone antagonist, results in reduced serum estradiol concentration and

no observation of hot flashes (page 97, lines 4-7). Thus, the working examples show how to treat, not how to prevent.

Note that lack of a working example to prevent, is a critical factor to be considered, especially in a case involving an unpredictable and undeveloped art. See MPEP 2164.

(8). ***Quantity of Experimentation Necessary***:

The specification fails to provide sufficient support of a preventive agent for hot flash. As a result, one of skill in the art would be forced to perform an exhaustive search for the embodiments of any drugs having the function recited in the instant claim suitable to practice the claimed invention.

Therefore, in view of the Wands factors, e.g. the predictability of the art, the amount of direction or guidence, and the lack of working examples discussed above, a person of skill in the art would not be able to fully practice the instant invention without ***undue experimentation***.

Claim Rejections - 35 USC § 103

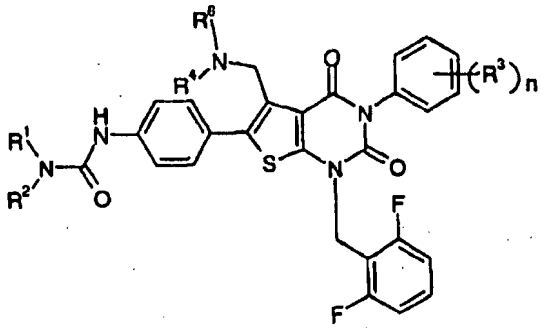
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,297,379) as evidenced by Hara et al. (The Journal of Clinical Endocrinology &

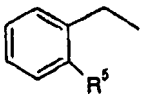
Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) and Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

Furuya et al. teach a method of treating sex hormone-dependent diseases comprising administering a compound of formula (I):



(I)

where R^6 is:



(abstract).

The compound of formula (I) has excellent gonadotropin releasing horomone (GnRH) antagonizing activity (abstract).

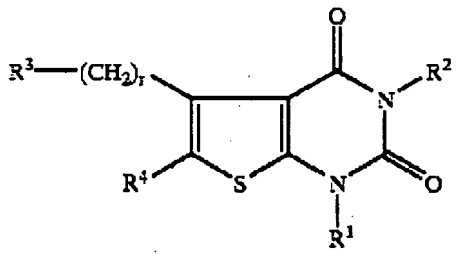
Regarding entering the brain as recited in instant claim 2, it is well known in the art that gonadotropin-releasing hormone (GnRH) is synthesized and released by the hypothalamus and is responsible for the release of follicle stimulating hormone (FSH) and lutenizing hormone (LH) from the anterior pituitary. It is also well known in the art that the anterior pituitary and hypothalamus are located at the brain stem. As evidenced by Hara et al., the gonadotropin-releasing hormone antagonist, TAK-013, was administered in female cynomolgus monkeys (page 1700). There was an LH surge in the plasma of monkeys treated with vehicle, however, there was no LH surge and LH plasma levels remained low in monkeys treated with TAK-013

(page 1700). Because gonadotropin-releasing hormone is synthesized in the hypothalamus, the gonadotropin-releasing hormone must reach and act in the brain in order to influence the release of lutenizing hormone. Thus it would be obvious that gonadotropin-releasing hormone enters the brain.

Regarding hot flash as recited in instant claim 7, Furuya et al. teach a method of treating sex hormone-dependent diseases (abstract). As evidenced by Freedman, hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a sex hormone-dependent condition.

6. Claims 2-5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,048,863) as evidenced by Hara et al. (The Journal of Clinical Endocrinology & Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) as applied to claim 2 above, and as further evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

Furuya et al. teach a method for treating disorders related to gonadotropin releasing hormone (GnRH) comprising administering a thienopyrimidine derivative of the formula:



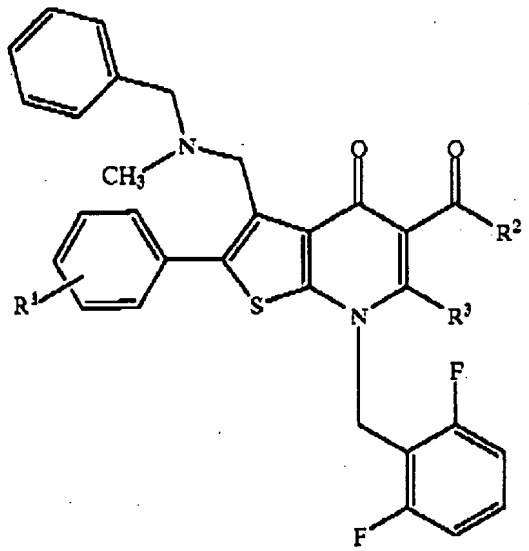
(abstract).

The thienopyrimidine derivative antagonizes gonadotropin-releasing hormone (column 2, lines 56-57).

Regarding hot flash as recited in instant claim 7, Furuya et al. teach a method of treating disorders related to gondotropin releasing hormone (abstract). As evidenced by Freedman, hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a disorder related to gonadotropin releasing hormone.

7. Claims 2-4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,001,850) as evidenced by Hara et al. (The Journal of Clinical Endocrinology & Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) and Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464) as applied to claims 2 and 7 above.

Furuya et al. teach a method for treating sex hormone dependent diseases comprising administering a thienopyridine derivative having gonadotropin-releasing hormone antagonistic activity of the formula:

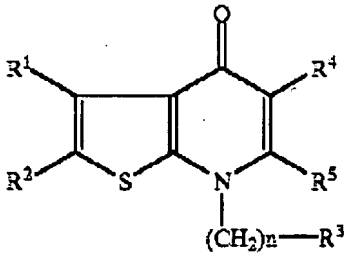


(abstract and column 36, lines 5-20).

The thienopyridine derivative has gonadotropin-releasing hormone antagonistic activity (abstract).

8. Claims 2-4 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Furuya et al. (US 6,187,788) as evidenced by Hara et al. (The Journal of Clinical Endocrinology & Metabolism, 2003, Vol. 88, No. 4, pp. 1697-1704) and Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464) as applied to claims 2 and 7 above.

Furuya et al. teach a method of treating a hormone dependent disease comprising administering a gonadotropin-releasing hormone antagonistic composition comprising a compound of the formula:



(abstract and column 116, lines 30-38).

Double Patenting

Obviousness-Type

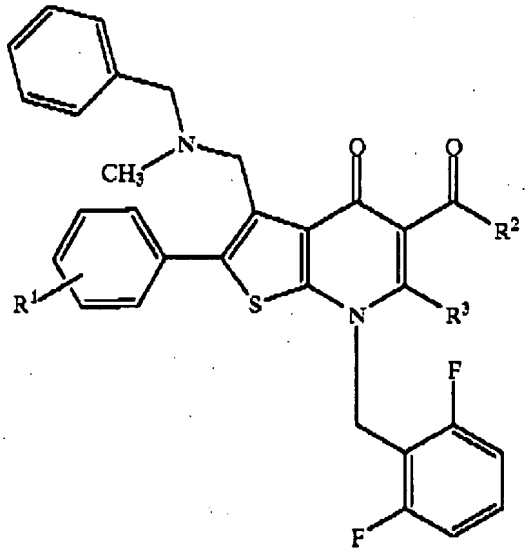
The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 4 and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 13 of Furuya et al. (US 6,001,850) as evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

Claim 13 of Furuya et al. is directed to a method of treating a gonadotropin-releasing hormone derived disorder comprising administering a compound of formula:

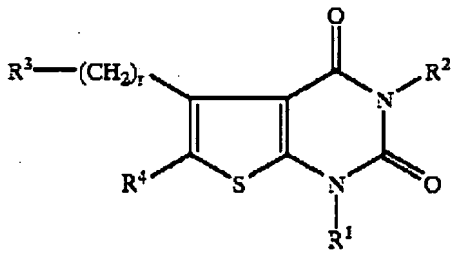


Freedman discloses that hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses

and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a gonadotropin-releasing hormone derived disorder.

10. Claims 4 and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 8 of Furuya et al. (US 6,048,863) as evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

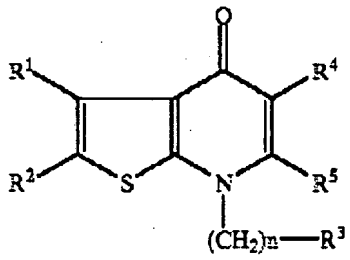
Claim 8 of Furuya et al. is directed to a method of treating a sex hormone dependent disease comprising administering a compound of formula:



Freedman discloses that hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a sex hormone dependent disease.

11. Claims 4 and 7 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4 of Furuya et al. (US 6,187,788) as evidenced by Freedman (American Journal of Human Biology, 2001, Vol. 13, pp. 453-464).

Claim 4 of Furuya et al. is directed at a method of treating a gonadotropin-releasing hormone dependent disorder comprising administering a compound of formula:



Freedman discloses that hot flashes most commonly occur with the estrogen withdrawal at menopause (abstract). Freedman further discloses that gonadotropins are elevated at menopause and that there was a temporal association found between lutenizing hormone pluses and hot flash occurrence (page 459). Thus it would be considered obvious that hot flashes are a gonadotropin-releasing hormone derived disorder.

Conclusion

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carlic K. Huynh whose telephone number is 571-272-5574. The examiner can normally be reached on Monday to Friday, 8:30AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

ckh

SHENGJUN WANG
PRIMARY EXAMINER